/alk, Roger A.

rom: Osborne, Kevin (PMMC Legal)
ent: Thursday, May 23, 2002 2:29 PM
o: Walk, Roger A.; Zhang, Mingda
c: Desel, Paula; 'Robert_Conley@aporter.com'
ubject: FW: <No subject>

oger and Mingda-

Pls. see the below note from Rob. He is currently drafting a section for best practices e toxicological assessments (IOM regulatory principles 7 & 8). Pls. consider the uestion he raises re process to complete the portion re how PM USA is applying or eeting the best practice. I agree w/ Rob's suggested approach but would appreciate your erspectives.

We should also consider how to best deal with this specific draft section, but hat will follow once we decide how to proceed generally.

Pls. let me know at your earliest convenience so we can proceed w/ finalizing nitial draft of this section and then distribute for comment.

hanks

----Original Message-----
rom: Robert_Conley@aporter.com [mailto:Robert_Conley@aporter.com]
ent: Wednesday, May 22, 2002 3:00 PM
o: Kevin.Osborne@us.pm.com
ubject: Re: <No subject>

evin -- per your e-mail (I'm not sure how concise this is):
As we have discussed the concept of what the best practices final product ight look like, we talked about how one part of the supporting materials might e a discussion of the underlying principles on which a given best practice was ased (e.g., the corresponding IOM regulatory principle, QS principles and PM ractices, etc.). For the most part, non-scientific persons (such as attorneys) ould initially draft these parts.

Another part might be a discussion of how PM would be applying or meeting he best practice -- not at a terribly detailed level, but providing the pproaches that might be used or alternatives that could meet the best practice. he goal would be to provide sufficient example and explanation so the best ractices and supporting materials could be a practical guide to implementation ithout locking in specific conclusions or becoming quickly outmoded.

For example, the toxicological assessment best practice says that appropriate" toxicological testing in preclinical laboratory and animal models ould be performed to support products with health-related claims. The IOM eport sets forth a general strategy for such testing (in vitro cytotoxicity and enotoxicity studies, followed by animal studies) that can be summarized in the irst part. But how will PM determine what testing is appropriate? What riteria will it use to make these determinations? These sorts of issues seem rimarily scientific (although with a regulatory overlay) and I'm not sure on-scientific folks are in the best position to draft a number of these types f discussions. There may be some limited exceptions. For example, based on he presentations a few weeks ago, we could probably draft something about how M defines various types of biomarkers. But there are aspects of biomarkers hat the presentation didn't cover. E.g., the IOM says biomarker assays should e validated by determining replicability (coefficient of variation), nterobserver and interlaboratory variability, and intraindividual and nterindividual variation. Is this going to be done? If so, are there any eneral guiding principles that should be stated (e.g., "intraindividual ariation can be measured by the following techniques, any of which may be

acceptable..." or "scientific literature can provide sufficient evidence" or ...)? If not, what is our rationale for not following the IOM Report? While scientific staff could educate us on all of the various aspects of all of the various best practices, it may be more efficient overall for appropriate scientific staff to take our draft discussions of the underlying principles and flesh them out.

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